Critical Review

Ligand Design for Functional Metal-Organic Frameworks

Filipe A. Almeida Paz,*[a] Jacek Klinowski,*[b]
Sérgio M. F. Vilela,[a,c] João P. C. Tomé[c]
José A. S. Cavaleiro[c] and João Rocha*[a]

A contribution from

[a] Department of Chemistry, CICECO, University of Aveiro,
Campus Universitário de Santiago, 3810-193 Aveiro, Portugal

[b] Department of Chemistry, University of Cambridge,
Lensfield Road, CB2 1EW Cambridge, U.K.

[c] Department of Chemistry, QOPNA, University of Aveiro,
Campus Universitário de Santiago, 3810-193 Aveiro, Portugal

Contacts:
E-mail filipe.paz@ua.pt
Telephone: +351 234370200, Extension 23553
Fax: +351 234370084

E-mail: jk18@hermes.cam.ac.uk
Telephone: +44 1223 336514
Fax: +44 1223 336362

Electronic Supporting Information
# Table of Contents

1 - Synthetic Procedures

1.1 - 4,4‘-Bipyridine-2,2‘-6,6'-tetracarboxylic acid ............................................................. 4
1.2 - Biphenyl-3,4',5-tricarboxylic acid ................................................................................. 4
1.3 - [1,4-Phenylenebis(methanetriyl)]tetraphosphonic acid .............................................. 5
1.4 - N,N'-Piperazinebis(methyleneephosphonic acid)
      2-Methyl-N,N'-piperazinebis(methyleneephosphonic acid) ........................................ 6
      2,5-Dimethyl-N,N'-piperazinebis(methyleneephosphonic acid) .................................. 6
1.5 - Azoxybenzene-3,3’,5,5’-tetracarboxylic acid ............................................................... 6
1.6 - trans-Stilbene-3,3’,5,5’-tetracarboxylic acid ................................................................. 7
1.7 - Azobenzene-3,3’,5,5’-tetracarboxylate ........................................................................ 7
1.8 - 1,3,5,7-Tetrakis(4-phophonophenyl)adamantane ......................................................... 8
1.9 - 4,5,9,10-Tetrahydropyrene-2,7-dicarboxylic acid ......................................................... 9
1.10 - 1,4-di(1H-Pyrazol-4-yl)benzene ................................................................................... 9
1.11 - 1,3,5-tris[4-(2H-Tetrazol-5-yl)phenyl]benzene
      2,4,6-tris[4-(2H-Tetrazol-5-yl)phenyl]-1,3,5-triazine ............................................... 10
1.12 - 5-(1H-Tetrazol-5-yl)isophthalic acid ......................................................................... 10
1.13 - 1,3,5-tris[1,3-Dicarboxylic acid-5-(4-ethylphenyl)ethyl]benzene ...................... 11
1.14 - 2-(1H-Tetrazol-5-yl)pyrimidine .................................................................................. 11
1.15 - 5-(4-Carboxyphenoxy)isophthalic acid .................................................................... 11
1.16 - Lithium 7,7’,8,8’-tetracyanoquinodimethanide(1-) .................................................. 12
1.17 - 1,2-bis[4-(Dicyanomethyl)]phenyl]ethane-1,1,2,2-tetracarbonitrile ....................... 12
1.18 - (S)-N-(Phosphonomethyl)proline .............................................................................. 12
1.19 - 3-[(E)-1,3,5-triazine-4,4′-bipyridyl]-4-hydroxybenzoic acid ............................... 13
1.20 - 4-Benzoyloxybenzonic acid
      4-Benzylmethyl-3-methoxybenzoic acid .................................................................. 13
1.21 - (5-Amino-1H-tetrazol-1-yl)acetic acid ..................................................................... 14
1.22 - 5-(1H-Tetrazol-5-yl)isothalatic acid (2nd route) ....................................................... 14
1.23 - N,N'-Di(4-pyridyl)-1,4,5,8-naphthalenetetracarboxydiimide ................................. 15
1.24 - 4,4‘,4”-Nitriolotrisbenzoic acid .............................................................................. 15
1.25 - 4,4‘,4”-4”-(Pyrene-1,3,6,8-tetrayl)tetrabenzoic acid .............................................. 16
1.26 - (4R,5R)-2,2-Dimethyl-5-[(pyridin-4-ylamino)carbonyl]-1,3-dioxolane-4-carboxylic acid ................................................................. 16
1.27 - 2,2'-Dihydroxy-1,1’-binaphthalene-6,6'-diphosphonic acid ..................................... 17
1.28 - N1’,N3’,N5’-tri(Pyridin-4-yl)benzene-1,3,5-tricarboxamide .................................... 17
1.29 - Tetrakis[4-(carboxyphenyl)oxymethyl]methane ...................................................... 18
1.30 - tris(2,3,5,6-Tetrachloro-4-carboxy)methyl radical .................................................. 19
1.31 - tris(2,4,6-Trichloro-3,5-dicarboxy)methyl radical ..................................................... 20
1.32 - 2,2′-Bipyridine-5,5′-dicarboxylic acid
Complexes:
Bromido-[(2,2′-bipyridine)-5,5′-dicarboxylic acid-k,N,N′]triscarbonylrhenium (I)
Chlorido-[(2,2′-bipyridine)-5,5′-dicarboxylic acid-k,N,N′]triscarbonylmanganese (I)........21

1.33 - 3-(Pyridin-2-yl)benzoic acid
Complexes:
4-(Pyridin-2-yl)benzoic acid
tris(3-(Pyridin-2-yl)benzoic acid-kN,kC)iridium (III)
tris(4-(Pyridin-2-yl)benzoic acid-kN,kC)iridium (III) .................................................................22

2 - References ....................................................................................................................23
1 - Synthetic Procedures

1.1 - 4,4’-Bipyridine-2,2’,6,6’-tetracarboxylic acid

![Chemical structure of 4,4’-bipyridine-2,2’,6,6’-tetracarboxylic acid]

i) Na, THF, r.t., N₂, 2-24 h (Caution: reaction under dry tetrahydrofuran!); ii) SO₂, 4-6 h; iii) H₂SO₄, CrO₃, 75 ºC, 2 h (Caution: care about chromium(VI) species as they are carcinogenic!).

**Figure S1** - Synthesis of 4,4’-bipyridine-2,2’,6,6’-tetracarboxylic acid according to Lin *et al.*

1.2 - Biphenyl-3,4’,5-tricarboxylic acid

![Chemical structure of biphenyl-3,4’,5-tricarboxylic acid]

i) a) Toluene, EtOH, K₂CO₃, H₂O; b) Pd(PPh₃)₄, reflux, N₂, overnight; ii) a) dioxane, KOH, reflux, 12 h; b) HCl.

**Figure S2** - Synthesis of biphenyl-3,4’,5-tricarboxylic acid according to Wong-Foy *et al.*
1.3 - [1,4-Phenylenebis(methanetriyl)]tetraphosphonic acid

Figure S3 - Synthesis of [1,4-phenylenebis(methanetriyl)]tetra-phosphonic acid according to Plabst and Bein.³
1.4 - $N,N'$-Piperazinebis(methyleneosphonic acid)
2-Methyl-$N,N'$-piperazinebis(methyleneosphonic acid)
2,5-Dimethyl-$N,N'$-piperazinebis(methyleneosphonic acid)

![Chemical structure]

$R^1 = H$ or $CH_3$
$R^2 = H$ or $CH_3$

i) $H_3PO_3$, HBr, $H_2O$, $CH_2O$, reflux, 20 h.

**Figure S4** - Synthesis of ($R^1 = H$ and $R^2 = H$) $N,N'$-piperazinebis(methyleneosphonic acid), according to Groves *et al.*, and of ($R^1 = CH_3$ and $R^2 = H$) 2-methyl-$N,N'$-piperazinebis(methyleneosphonic acid) and ($R^1 = CH_3$ and $R^2 = CH_3$) 2,5-dimethyl-$N,N'$-piperazinebis(methylene-phosphonic acid) according to Mowat *et al.*

1.5 - Azoxybenzene-3,3',5,5'-tetracarboxylic acid

![Chemical structure]

i) Zn, NaOH, EtOH, $H_2O$, reflux, 12h.

**Figure S5** - Synthesis of azoxybenzene-3,3',5,5'-tetracarboxylic acid according to Wang *et al.*
1.6 - trans-Stilbene-3,3′,5,5′-tetracarboxylic acid

\[
\text{HO}_2\text{C} - \text{CO}_2\text{H} \quad \text{Br} \quad \text{HO}_2\text{C} - \text{CO}_2\text{H} \quad \text{MeO}_2\text{C} - \text{CO}_2\text{Me}
\]

i) Br_2, H_2SO_4 (Caution: bromine is highly toxic by inhalation!); ii) MeOH, H_2SO_4; iii) Pd(OAc)_2 (1 mol%), Pd(α-Toly)_3 (1 mol%), NMP, Et_3N, ethene (1.5 bar), 100 °C, 25.5 h; iv) a) NaOH, THF, MeOH; b) HCl.

**Figure S6** - Synthesis of trans-stilbene-3,3′,5,5′-tetracarboxylic acid according to Wang et al.⁶

1.7 - Azobenzene-3,3′,5,5′-tetracarboxylate

\[
\text{HO}_2\text{C} - \text{CO}_2\text{H} \quad \text{N} - \text{N} - \text{CO}_2\text{H} \quad \text{O}_2\text{C} - \text{N} - \text{N} - \text{CO}_2\text{H}
\]

i) Reduction under solvothermal conditions.

**Figure S7** - Synthesis of azobenzene-3,3′,5,5′-tetracarboxylate according to Wang et al.⁶
1.8 - 1,3,5,7-Tetrakis(4-phosphonophenyl)adamantane

![Chemical structure](image)

i) PdCl$_2$(PPh$_3$)$_2$, HPO(OEt)$_2$, Et$_3$N, benzene, 80 ºC, 72 h; ii) HCl, reflux, 24 h.

**Figure S8** - Synthesis of 1,3,5,7-tetrakis(4-phosphonophenyl)adamantane according to Vasylyev *et al.*

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1.9 - 4,5,9,10-Tetrahydropyrene-2,7-dicarboxylic acid

![Chemical structure](image1)

1) a) Raney nickel, EtOAc, 2 d (Caution: do not let the Raney nickel became dry!); b) H₂ (45 psi.), 10% Pd/C, EtOAc, 3 d; ii) AcCl, AlCl₃, CH₂Cl₂, N₂, 0 ºC to r.t., 2.5 h (Caution: AlCl₃ releases HCl fumes!); iii) Br₂, NaOH, dioxane/water (Caution: bromine is highly toxic by inhalation!).

Figure S9 - Synthesis of 4,5,9,10-tetrahydropyrene-2,7-dicarboxylic acid according to Connor et al.⁸

1.10 - 1,4-di(1H-Pyrazol-4-yl)benzene

![Chemical structure](image2)

i) DMF, POCl₃, 90-95 ºC, 4 h (Caution: phosphoryl chloride can release HCl fumes!); ii) NaClO₄; iii) a) NaOH, 90 ºC, 7-8 min; b) HCl; iv) N₂H₄, r.t., 15-20 min.

Figure S10 - Synthesis of 1,4-di(1H-pyrazol-4-yl)benzene according to Lozan et al.⁹
1.11 - 1,3,5-tris[4-(2H-Tetrazol-5-yl)phenyl]benzene
2,4,6-tris[4-(2H-Tetrazol-5-yl)phenyl]-1,3,5-triazine

\[
\begin{align*}
\text{i) } & \text{CuCN, DMF, reflux, N}_2, \text{ 24 h (Caution: do not let reactions with cyanide salts become acid. HCN is highly toxic by inhalation!); ii) a) NaN}_3, \text{Et}_3\text{N} \cdot \text{HCl, toluene, MeOH, reflux, 4 d; b) NaOH, r.t., 30 min (Caution: metal azides and tetrazoles are potentially explosive and should be handled with great care!).} \\
\end{align*}
\]

**Figure S11** - Synthesis of \((Z = \text{CH})\) 1,3,5-tris[4-(2H-tetrazol-5-yl)phenyl]benzene and \((Z = \text{N})\) 2,4,6-tris[4-(2H-tetrazol-5-yl)phenyl]-1,3,5-triazine according to Dincă *et al.*

1.12 - 5-(1H-Tetrazol-5-yl)isophthalic acid

\[
\begin{align*}
\text{i) } & \text{HCl, NaNO}_2, \text{ 0 ºC; ii) NaCN, CuCN, reflux, 40 min (Caution: do not let reactions with cyanide salts become acid. HCN is highly toxic by inhalation!); iii) NaN}_3, \text{ZnBr}_2, \text{H}_2\text{O, reflux, 24 h (Caution: metal azides and tetrazoles are explosive and should be handled with great care!).} \\
\end{align*}
\]

**Figure S12** - Synthesis of 5-(1H-tetrazol-5-yl)isophthalic acid according to Demko *et al.* and Ritzen *et al.*
1.13 - 1,3,5-tris[(1,3-Dicarboxylic acid-5-(4-(ethynyl)phenyl))ethynyl]benzene

![Chemical structure of 1,3,5-tris[(1,3-Dicarboxylic acid-5-(4-(ethynyl)phenyl))ethynyl]benzene](image)

**Figure S13** - For a detailed synthetic procedure of 1,3,5-tris[(1,3-dicarboxylic acid-5-(4-(ethynyl)phenyl))ethynyl]benzene see the Electronic Supporting Information of the paper by Farha *et al.*¹³

1.14 - 2-(1H-Tetrazol-5-yl)pyrimidine

![Chemical structure of 2-(1H-tetrazol-5-yl)pyrimidine](image)

i) NaN₃, MeOH, r.t. (Caution: metal azides and tetrazoles are potentially explosive and should be handled with great care!).

**Figure S14** - Synthesis of 2-(1H-tetrazol-5-yl)pyrimidine according to Pachfule *et al.*¹⁴

1.15 - 5-(4-Carboxyphenoxy)isophthalic acid

![Chemical structures of 5-(4-carboxyphenoxy)isophthalic acid](image)

i) K₂CO₃, DMF, 80 °C, 24 h; ii) NaOH, reflux: iii) HCl.

**Figure S15** - Synthesis of 5-(4-carboxyphenoxy)isophthalic acid according to Lama *et al.*¹⁵
1.16 - Lithium 7,7',8,8'-tetracyanoquinodimethanide(1-)

![Chemical structure diagram]

i) CNCH₂CN, CH₃COOH, CH₃COONH₄, reflux, 2 h; ii) Br₂, CH₃CN, C₅H₅N, 20 °C, N₂, 1 h (Caution: bromine is highly toxic by inhalation!); iii) LiI, CH₃CN.

Figure S16 - Synthesis of lithium 7,7',8,8'-tetracyanoquinodimethanide(1-) according to Acker and Hertler¹⁶ and Cornelissen et al.¹⁷

1.17 - 1,2-bis[4-(Dicyanomethyl)phenyl]ethane-1,1,2,2-tetracarbonitrile

![Chemical structure diagram]

i) TCNQ dimer was derived in situ, under solvothermal conditions, from σ dimerization of two TCNQ' anions.

Figure S17 - Synthesis of 1,2-bis[4-(dicyanomethyl)phenyl]ethane-1,1,2,2-tetracarbonitrile according to Shimomura et al.¹⁸

1.18 - (S)-N-(Phosphonomethyl)proline

![Chemical structure diagram]

i) H₃PO₃, HCl, CH₂O, reflux, 90 min; ii) ethanol, reflux.

Figure S18 - Synthesis of (S)-N-(phosphonomethyl)proline according to Yue et al.¹⁹
1.19 - 3-[[E]-[[1R,2R]-2-Aminocyclohexyl[jmino]methyl]-4-hydroxybenzoic acid

![Reaction Scheme]

i) CHCl₃, NaOH; ii) HCl; iii) MeOH, reflux, 1 h.

Figure S19 - Synthesis of 3-[[E]-[[1R,2R]-2-aminocyclohexyl[jmino]methyl]-4-hydroxybenzoic acid according to Yuan et al.²⁰

1.20 - 4-Benzylxybenzoic acid
4-Benzylxy-3-methoxybenzoic acid
4-Benzylxy-3-nitrobenzoic acid

![Reaction Scheme]

R = -H, -OMe or -NO₂

i) H₂SO₄, MeOH, 24h, 68 °C; ii) K₂CO₃, C₆H₅-CH₂Br, DMF, 48h, 78 °C; iii) KOH, EtOH, 24h, 68 °C.

Figure S20 - Synthesis of (R = H) 4-benzylxybenzoic, (R = OCH₃) 4-benzylxy-3-methoxybenzoic and (R = NO₂) 4-benzylxy-3-nitrobenzoic acids according to Sivakumar et al.²¹
1.21 - (5-Amino-1H-tetrazol-1-yl)acetic acid

\[ \text{N} \equiv \text{NH} \rightarrow \text{N=NH} \]

i) CICH₂COOH, KOH, CH₃OH, reflux, 18-24 h (Caution: tetrazoles are potentially explosive and should be handled with great care!).

**Figure S21** - Synthesis of (5-amino-1H-tetrazol-1-yl)acetic acid according to Einberg²² and Li et al.²³

1.22 - 5-(1H-Tetrazol-5-yl)isophtalic acid (2nd route)

\[ \text{CHO} \rightarrow \text{CN} \]

i) Ce(NH₄)₂(NO₃)₆, CH₃COOH; ii) THF, NH₄OH, I₂; iii) NaN₃, NH₄Cl, DMF (Caution: metal azides and tetrazoles are potentially explosive and should be handled with great care!); iv) KMnO₄.

**Figure S22** - A different synthesis of 5-(1H-tetrazol-5-yl)isophtalic acid according to Qu et al.²⁴
1.23 - \(N,N'-\text{Di-(4-pyridyl)-1,4,5,8-naphthalenetetracarboxydiimide}\)

![Diagram of N,N'-Di-(4-pyridyl)-1,4,5,8-naphthalenetetracarboxydiimide synthesis]

Figure S23 - Synthesis of \(N,N'-\text{Di-(4-pyridyl)-1,4,5,8-naphthalenetetracarboxydiimide}\) according to Dinolfo et al. 

1.24 - 4,4',4''-Nitrilotrisbenzoic acid

![Diagram of 4,4',4''-Nitrilotrisbenzoic acid synthesis]

Figure S24 - Synthesis of 4,4’,4’’-nitrilotrisbenzoic acid according to Dapperheld et al.
**1.25 - 4,4',4'',4'''-(Pyrene-1,3,6,8-tetrayl)tetrabenzoic acid**

![Chemical structure diagram](image1)

i) Nitrobenzene, Br₂, 120 °C, 14 h (Caution: nitrobenzene and bromine are highly toxic by inhalation!); ii) a) Pd(PPh₃)₄, K₂CO₃, dry dioxane, N₂, 85 °C, 72 h; b) H₂O/HCl (3:1); iii) a) NaOH, THF/dioxane/H₂O (5:2:2), 85 °C, overnight; b) H₂O, HCl.

**Figure S25** - Synthesis of 4,4',4'',4'''-(pyrene-1,3,6,8-tetrayl)tetrabenzoic acid according to Stylianou et al.²⁷

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**1.26 - (4R,5R)-2,2-Dimethyl-5-[(pyridin-4-ylamino)carbonyl]-1,3-dioxolane-4-carboxylic acid**

![Chemical structure diagram](image2)

i) DCC, CH₂Cl₂, r.t., 5 h; ii) KOH, MeOH, reflux, 8 h.

**Figure S26** - Synthesis of (4R,5R)-2,2-dimethyl-5-[(pyridin-4-ylamino)carbonyl]-1,3-dioxolane-4-carboxylic acid according to Seo et al.²⁸ (for the final product), and Musich and Rapoport²⁹ (for the starting chemical).
1.27 - 2,2'-Diethoxy-1,1'-binaphthalene-6,6'-diphosphonic acid

\[
\text{EtO} - \begin{array}{c}
\text{Br} \\
\text{EtO}
\end{array} \quad \text{+} \quad \begin{array}{c}
\text{EtO} \\
\text{Br}
\end{array} \rightarrow \text{EtO} - \begin{array}{c}
\text{PO}_{3}\text{Et}_{2}
\end{array}
\]

\(i)\ Pd(PPh_{3})_{4}, \text{dry toluene, Et}_{3}N, \text{reflux, N}_{2}, \text{48 h}\); \(ii)\ a) \text{Me}_{3}\text{SiBr, CH}_{2}\text{Cl}_{2, \text{r.t, N}_{2}, \text{24 h}}\); b) \text{MeOH}.

**Figure S27** - Synthesis of 2,2'-diethoxy-1,1'-binaphthalene-6,6'-diphosphonic acid according to Evans *et al.*\(^{30,31}\)

1.28 - \(N^1,N^3,N^5\)-tri(Pyridin-4-yl)benzene-1,3,5-tricarboxamide

\[
\begin{array}{c}
\text{N} \\
\text{NH}_{2}
\end{array} \quad \text{+} \quad \begin{array}{c}
\text{O} \\
\text{Cl} \\
\text{Cl}
\end{array} \rightarrow \begin{array}{c}
\text{OH} \\
\text{NH} \\
\text{O}
\end{array}
\]

\(i)\ Et_{3}N, \text{THF, r.t, 7 h (Caution: aniline should be handled carefully!)}.\)

**Figure S28** - Synthesis of \(N^1,N^3,N^5\)-tri(pyridin-4-yl)benzene-1,3,5-tricarboxamide according to Hasegawa *et al.*\(^{32}\)
1.29 - Tetrakis[4-(carboxyphenyl)oxymethyl]methane

i) $\text{K}_2\text{CO}_3$, DMF, 90 °C, 92 h; ii) KOH, EtOH, THF, reflux, 2 h.

Figure S29 - Synthesis of tetrakis[4-(carboxyphenyl)oxymethyl]-methane according to Tu et al.³³
1.30 - tris(2,3,5,6-Tetrachloro-4-carboxy)methyl radical

\[
\begin{align*}
\text{i) } & \text{CHCl}_3, \text{AlCl}_3 \text{ (Caution: aluminum chloride reacts vigorously with water and releases HCl fumes. Dry conditions are required!); ii) fuming sulfuric acid (Caution: H}_2\text{SO}_4 \text{ is highly corrosive!); iii) NaOH, I}_2, \text{HCl.}} \\
\end{align*}
\]

**Figure S30** - Synthesis of tris(2,3,5,6-tetrachloro-4-carboxy)methyl radical according to Maspoch *et al.*
**1.31 - tris(2,4,6-Trichloro-3,5-dicarboxy)methyl radical**

![Chemical structure diagram]

i) CH$_3$Cl, AlCl$_3$ (Caution: aluminum chloride reacts vigorously with water and releases HCl fumes. Dry conditions are required!); ii) fuming sulfuric acid (Caution: H$_2$SO$_4$ is highly corrosive!); iii) CH$_2$N$_2$ (Caution: diazomethane is highly toxic by inhalation or skin and eyes contact!); iv) Bu$_4$NOH, $p$-chloranil; v) H$_2$SO$_4$.

**Figure S31** - Synthesis of tris(2,4,6-trichloro-3,5-dicarboxy)methyl radical according to Roques et al.$^{35}$
1.32 - 2,2′-Bipyridine-5,5′-dicarboxylic acid

Complexes:
- Bromido-[(2,2′-bipyridine)-5,5′-dicarboxylic acid-k-N,N′]triscarbonylrhenium (I)
- Chlorido-[(2,2′-bipyridine)-5,5′-dicarboxylic acid-k-N,N′]triscarbonylmanganese (I)

**Figure S32 - Synthesis of 2,2′-bipyridine-5,5′-dicarboxylic acid [step i]), according to Nelissen et al.\textsuperscript{36} and Venema et al.,\textsuperscript{37} and of its complexes [step ii) or iii)] according to Blake et al.\textsuperscript{38}**
1.33 - 3-(Pyridin-2-yl)benzoic acid and 4-(Pyridin-2-yl)benzoic acid

Complexes:
tris(3-(Pyridin-2-yl)benzoic acid-kN,kC')iridium (III)
tris(4-(Pyridin-2-yl)benzoic acid-kN,kC')iridium (III)

Figure S33 - Synthesis of 3-(pyridin-2-yl)benzoic acid and 4-(pyridin-2-yl)benzoic acid, and of their complexes with iridium (III) according to Xie et al.39
2 - References


